

**NMR Spectroscopic Windows on the Systemic Effects of SARS-CoV-2 Infection on Plasma
Lipoproteins and Metabolites in Relation to Circulating Cytokines**

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Table S1a - Full cohort demographic data.

	SARS-CoV-2 Positive (+) (N=15)	Healthy Controls (N=27)	SARS-CoV-2 Negative (-) Hospitalised (N = 11)	SARS-CoV-2 Negative (-) Non- Hospitalised (N = 24)	Serology detected (N=7)
Sex, Male	11 (58.82%)	16 (59.26%)	5 (45.45%)	11 (45.83%)	5 (71.43%)
Age, years [SD]	68.20 [±11.54]	52.74 [± 15.06]	67.45 [±21.03]	48.63 [±15.85]	62.71 [±18.49]
BMI, kg/m ² [SD]	34.66 [±11.85]	26.13[± 3.42]	25.73 [± 5.01]	29.6 [± 7.82]	26.17 [±4.07]
Pre-diabetic/diabetic	2 (13.33%)	2 (7.41%)	1 (4.54%)	3 (12.5%)	0
Hypertension	7 (46.67%)	2 (7.41%)	0	5 (20.83%)	3 (42.85%)
Asthma	3 (20.00%)	0	0	6 (25.00%)	0
COPD	1 (6.67%)	0	2 (9.09%)	1 (4.17%)	0
Arthritis	4 (26.67%)	0	0	0	0
Glaucoma	2 (13.33%)	0	0	0	0
Dyslipidaemia	1 (6.67%)	0	0	0	0
Chronic Renal Disease	2 (13.33%)	0	3 (13.64%)	0	0
Chronic heart disease	1 (6.67%)	0	2 (9.09%)	0	0

Table S1b - Cohort demographic data for the training set.

	SARS-Cov2 positive patients (n=7)	Healthy controls (n=7)
Male sex	3 (42.86%)	4 (57.1%)
Age, years [SD]	64.6 [±13.13]	65.0 [±13.1]
BMI, kg/m ² [SD]	37.49 [±10.56]	25.7 [±4.1]
Pre diabetic/diabetic	1	0
Hypertension	4 (57.1%)	1 (14.3%)
Asthma	1 (14.3%)	0

Chronic obstructive pulmonary disease	0	0
Arthritis	1 (14.3%)	0
Glaucoma	1 (14.3%)	0
Dyslipidaemia	0	0
Chronic Renal Disease	0	0
Chronic heart disease	1 (14.3%)	0

Table S2 - Symptoms presentation in SARS-CoV-2 positive patients.

Symptom	SARS-Cov2 positive patients (n=15)
Fever	8 (53.3%)
Cough	9 (60.0%)
Shortness of breath	6 (40.0%)
Sore throat	1 (6.7%)
Rhinorrhoea	2 (13.3%)
Wheeze	1 (6.7%)
Chest pain	1 (6.7%)
Myalgia	2 (13.3%)
Joint pain	1 (6.7%)
Fatigue	5 (33.3%)
Headache	2 (13.3%)
Confusion	2 (13.3%)
Abdominal pain	1 (6.7%)
Vomit	2 (13.3%)
Diarrhoea	3 (20.0%)
Conjunctivitis	0
Lymphadenopathy	0

Table S3 – Serology IgA and IgG concentrations

Group	IgA mean (+/- StDev)	IgG mean (+/- StDev)
SARS-CoV-2 positive	Beyond detection limit*	6.61 (+/-4.49)
SARS-CoV-2 negative	0.33 (+/-0.16)	0.12 (+/-0.09)
Control (seronegative)	0.25 (+/-0.19)	0.09 (+/-0.07)
Control (seropositive)	1.90 (+/-0.89)	0.30 (+/-0.26)

*5 of 9 samples were above the detection limit of 10.2 with the other 4 samples reading from 1.0 to 6.1 and therefore the true mean could not be calculated.

Table S4 - Annotation of the keys used by the Bruker IVDr Lipoprotein Subclass Analysis (B.I.-LISA™) method. Abbreviations: LDL – low-density lipoprotein; HDL – high-density lipoprotein; VLDL – very low-density lipoprotein; IDL – intermediate-density lipoprotein.

Key	Class/subclass	Compound	Concentration unit
TPTG	Total Plasma	Triglycerides	mg/dL
TPCH	Total Plasma	Cholesterol	mg/dL
LDCH	LDL	Cholesterol	mg/dL
HDCH	HDL	Cholesterol	mg/dL
TPA1	Total Plasma	Apolipoprotein-A1	mg/dL
TPA2	Total Plasma	Apolipoprotein-A2	mg/dL
TPAB	Total Plasma	Apolipoprotein-B100	mg/dL
LDHD	Ratio LDL and HDL	LDL Cholesterol / HDL	-/-
	Cholesterol	Cholesterol	
ABA1	Ratio of Apolipoproteins A1 and B100	Apolipoprotein-A1 / Apolipoprotein-B100	-/-
TBPN	Apolipoprotein-B100 carrying particles	Particle Number	nmol/L
VLPN	VLDL	Particle Number	nmol/L
IDPN	IDL	Particle Number	nmol/L
LDPN	LDL	Particle Number	nmol/L
L1PN	LDL-1	Particle Number	nmol/L
L2PN	LDL-2	Particle Number	nmol/L

L3PN	LDL-3	Particle Number	nmol/L
L4PN	LDL-4	Particle Number	nmol/L
L5PN	LDL-5	Particle Number	nmol/L
L6PN	LDL-6	Particle Number	nmol/L
VLTG	VLDL Class	Triglycerides	mg/dL
IDTG	IDL Class	Triglycerides	mg/dL
LDTG	LDL Class	Triglycerides	mg/dL
HDTG	HDL Class	Triglycerides	mg/dL
VLCH	VLDL Class	Cholesterol	mg/dL
IDCH	IDL Class	Cholesterol	mg/dL
LDCH	LDL Class	Cholesterol	mg/dL
HDCH	HDL Class	Cholesterol	mg/dL
VLFC	VLDL Class	Free Cholesterol	mg/dL
IDFC	IDL Class	Free Cholesterol	mg/dL
LDFC	LDL Class	Free Cholesterol	mg/dL
HDFC	HDL Class	Free Cholesterol	mg/dL
VLPL	VLDL Class	Phospholipids	mg/dL
IDPL	IDL Class	Phospholipids	mg/dL
LDPL	LDL Class	Phospholipids	mg/dL
HDPL	HDL Class	Phospholipids	mg/dL
HDA1	HDL Class	Apolipoprotein-A1	mg/dL
HDA2	HDL Class	Apolipoprotein-A2	mg/dL
VLAB	VLDL Class	Apolipoprotein-B100	mg/dL
IDAB	IDL Class	Apolipoprotein-B100	mg/dL
LDAB	LDL Class	Apolipoprotein-B100	mg/dL
V1TG	VLDL-1 Subclass	Triglycerides	mg/dL
V2TG	VLDL-2 Subclass	Triglycerides	mg/dL
V3TG	VLDL-3 Subclass	Triglycerides	mg/dL
V4TG	VLDL-4 Subclass	Triglycerides	mg/dL
V5TG	VLDL-5 Subclass	Triglycerides	mg/dL
V1CH	VLDL-1 Subclass	Cholesterol	mg/dL
V2CH	VLDL-2 Subclass	Cholesterol	mg/dL
V3CH	VLDL-3 Subclass	Cholesterol	mg/dL

V4CH	VLDL-4 Subclass	Cholesterol	mg/dL
V5CH	VLDL-5 Subclass	Cholesterol	mg/dL
V1FC	VLDL-1 Subclass	Free Cholesterol	mg/dL
V2FC	VLDL-2 Subclass	Free Cholesterol	mg/dL
V3FC	VLDL-3 Subclass	Free Cholesterol	mg/dL
V4FC	VLDL-4 Subclass	Free Cholesterol	mg/dL
V5FC	VLDL-5 Subclass	Free Cholesterol	mg/dL
V1PL	VLDL-1 Subclass	Phospholipids	mg/dL
V2PL	VLDL-2 Subclass	Phospholipids	mg/dL
V3PL	VLDL-3 Subclass	Phospholipids	mg/dL
V4PL	VLDL-4 Subclass	Phospholipids	mg/dL
V5PL	VLDL-5 Subclass	Phospholipids	mg/dL
L1TG	LDL-1 Subclass	Triglycerides	mg/dL
L2TG	LDL-2 Subclass	Triglycerides	mg/dL
L3TG	LDL-3 Subclass	Triglycerides	mg/dL
L4TG	LDL-4 Subclass	Triglycerides	mg/dL
L5TG	LDL-5 Subclass	Triglycerides	mg/dL
L6TG	LDL-6 Subclass	Triglycerides	mg/dL
L1CH	LDL-1 Subclass	Cholesterol	mg/dL
L2CH	LDL-2 Subclass	Cholesterol	mg/dL
L3CH	LDL-3 Subclass	Cholesterol	mg/dL
L4CH	LDL-4 Subclass	Cholesterol	mg/dL
L5CH	LDL-5 Subclass	Cholesterol	mg/dL
L6CH	LDL-6 Subclass	Cholesterol	mg/dL
L1FC	LDL-1 Subclass	Free Cholesterol	mg/dL
L2FC	LDL-2 Subclass	Free Cholesterol	mg/dL
L3FC	LDL-3 Subclass	Free Cholesterol	mg/dL
L4FC	LDL-4 Subclass	Free Cholesterol	mg/dL
L5FC	LDL-5 Subclass	Free Cholesterol	mg/dL
L6FC	LDL-6 Subclass	Free Cholesterol	mg/dL
L1PL	LDL-1 Subclass	Phospholipids	mg/dL
L2PL	LDL-2 Subclass	Phospholipids	mg/dL
L3PL	LDL-3 Subclass	Phospholipids	mg/dL

L4PL	LDL-4 Subclass	Phospholipids	mg/dL
L5PL	LDL-5 Subclass	Phospholipids	mg/dL
L6PL	LDL-6 Subclass	Phospholipids	mg/dL
L1AB	LDL-1 Subclass	Apolipoprotein-B100	mg/dL
L2AB	LDL-2 Subclass	Apolipoprotein-B100	mg/dL
L3AB	LDL-3 Subclass	Apolipoprotein-B100	mg/dL
L4AB	LDL-4 Subclass	Apolipoprotein-B100	mg/dL
L5AB	LDL-5 Subclass	Apolipoprotein-B100	mg/dL
L6AB	LDL-6 Subclass	Apolipoprotein-B100	mg/dL
H1TG	HDL-1 Subclass	Triglycerides	mg/dL
H2TG	HDL-2 Subclass	Triglycerides	mg/dL
H3TG	HDL-3 Subclass	Triglycerides	mg/dL
H4TG	HDL-4 Subclass	Triglycerides	mg/dL
H1CH	HDL-1 Subclass	Cholesterol	mg/dL
H2CH	HDL-2 Subclass	Cholesterol	mg/dL
H3CH	HDL-3 Subclass	Cholesterol	mg/dL
H4CH	HDL-4 Subclass	Cholesterol	mg/dL
H1FC	HDL-1 Subclass	Free Cholesterol	mg/dL
H2FC	HDL-2 Subclass	Free Cholesterol	mg/dL
H3FC	HDL-3 Subclass	Free Cholesterol	mg/dL
H4FC	HDL-4 Subclass	Free Cholesterol	mg/dL
H1PL	HDL-1 Subclass	Phospholipids	mg/dL
H2PL	HDL-2 Subclass	Phospholipids	mg/dL
H3PL	HDL-3 Subclass	Phospholipids	mg/dL
H4PL	HDL-4 Subclass	Phospholipids	mg/dL
H1A1	HDL-1 Subclass	Apolipoprotein-A1	mg/dL
H2A1	HDL-2 Subclass	Apolipoprotein-A1	mg/dL
H3A1	HDL-3 Subclass	Apolipoprotein-A1	mg/dL
H4A1	HDL-4 Subclass	Apolipoprotein-A1	mg/dL
H1A2	HDL-1 Subclass	Apolipoprotein-A2	mg/dL
H2A2	HDL-2 Subclass	Apolipoprotein-A2	mg/dL
H3A2	HDL-3 Subclass	Apolipoprotein-A2	mg/dL
H4A2	HDL-4 Subclass	Apolipoprotein-A2	mg/dL

Table S5 – Lipoprotein OPLS-DA training model loadings and Cliff's delta for all lipoprotein subfractions. Ranked by Cliff's delta.

Rank	Lipoprotein subfraction	Loadings from OPLS-DA	Cliff's delta	P value
1	TPA1	0.18	1.00	0.0017
2	HDA1	0.18	1.00	0.0017
3	HDCH	0.17	0.92	0.0040
4	TPA2	0.18	0.92	0.0040
5	HDFC	0.16	0.88	0.0060
6	HDA2	0.17	0.88	0.0060
7	H3FC	0.17	0.88	0.0060
8	ABA1	0.16	-0.88	0.0059
9	H4CH	0.18	0.84	0.0088
10	H4FC	0.17	0.84	0.0088
11	H4A1	0.17	0.84	0.0088
12	H3CH	0.15	0.80	0.0127
13	H4PL	0.18	0.80	0.0127
14	H4A2	0.15	0.80	0.0127
15	HDPL	0.15	0.76	0.0181
16	TPCH	0.15	0.71	0.0253
17	H3A1	0.15	0.71	0.0253
18	LDHD	0.12	-0.71	0.0253
19	L4TG	0.15	-0.71	0.0253
20	H2A1	0.13	0.67	0.0350
21	V4FC	0.11	-0.67	0.0350
22	L5TG	0.15	-0.67	0.0350
23	H1FC	0.14	0.63	0.0476
24	H3PL	0.13	0.63	0.0476
25	L2TG	0.14	-0.61	0.0550
26	IDPN	0.12	-0.59	0.0639
27	LDTG	0.15	-0.59	0.0639
28	IDAB	0.12	-0.59	0.0639
29	H2FC	0.09	0.55	0.0845

30	H3A2	0.09	0.47	0.1417
31	VLPN	0.08	-0.47	0.1417
32	VLAB	0.08	-0.47	0.1417
33	V4CH	0.07	-0.47	0.1413
34	V4PL	0.09	-0.47	0.1417
35	L1TG	0.13	-0.47	0.1417
36	H1CH	0.12	0.43	0.1797
37	V4TG	0.07	-0.43	0.1797
38	V2FC	0.07	-0.43	0.1797
39	TPAB	0.04	-0.39	0.2248
40	TBPN	0.04	-0.39	0.2248
41	L6TG	0.05	-0.37	0.2496
42	L1CH	0.07	0.35	0.2774
43	L2CH	0.05	0.35	0.2774
44	H2CH	0.10	0.35	0.2774
45	IDCH	0.08	-0.35	0.2774
46	IDFC	0.08	-0.35	0.2774
47	V3CH	0.08	-0.35	0.2774
48	V3FC	0.07	-0.35	0.2774
49	V3PL	0.07	-0.35	0.2774
50	H2TG	0.10	-0.35	0.2769
51	H3TG	0.09	-0.35	0.2769
52	LDPN	0.02	-0.31	0.3379
53	LDAB	0.02	-0.31	0.3379
54	L3TG	0.08	-0.31	0.3379
55	V5FC	0.07	0.29	0.3695
56	V5CH	0.07	0.27	0.4062
57	L3FC	0.05	0.27	0.4062
58	L6FC	0.11	0.27	0.4062
59	H1A1	0.11	0.27	0.4062
60	H2A2	0.06	0.27	0.4062
61	LDCH	0.07	0.22	0.4822
62	V3TG	0.03	-0.27	0.4062

63	LDFC	0.06	0.22	0.4822
64	V5PL	0.06	0.22	0.4822
65	L1FC	0.05	0.22	0.4822
66	L2FC	0.04	0.22	0.4822
67	L2PL	0.02	0.22	0.4822
68	H4TG	0.03	0.22	0.4822
69	H2PL	0.06	0.22	0.4822
70	VLCH	0.02	-0.22	0.4822
71	IDTG	0.05	0.18	0.5653
72	L3CH	0.04	0.18	0.5653
73	L6PL	0.09	0.18	0.5653
74	H1A2	0.09	0.18	0.5653
75	L1PN	0.05	-0.18	0.5653
76	V5TG	0.01	-0.18	0.5653
77	V2CH	0.02	-0.18	0.5653
78	L1AB	0.05	-0.18	0.5653
79	IDPL	0.06	0.14	0.6547
80	L4CH	0.02	0.14	0.6547
81	H1PL	0.10	0.14	0.6547
82	L3PN	0.03	-0.14	0.6547
83	L4PN	0.03	-0.14	0.6547
84	VLPL	0.01	-0.14	0.6547
85	V1TG	0.03	-0.14	0.6547
86	L3AB	0.03	-0.14	0.6547
87	L4AB	0.03	-0.14	0.6547
88	L5PL	0.00	0.12	0.7012
89	LDPL	0.05	0.10	0.7494
90	L5CH	0.02	0.10	0.7494
91	L5FC	0.02	0.10	0.7494
92	L3PL	0.02	0.10	0.7494
93	TPTG	0.01	-0.10	0.7494
94	VLTG	0.01	-0.10	0.7494
95	VLFC	0.01	-0.10	0.7494

96	V2TG	0.00	-0.10	0.7494
97	V2PL	0.01	-0.10	0.7494
98	L6PN	0.07	0.06	0.8480
99	L6CH	0.08	0.06	0.8480
100	L1PL	0.02	0.06	0.8480
101	L6AB	0.07	0.06	0.8480
102	H1TG	0.00	0.06	0.8480
103	L2PN	0.03	-0.06	0.8480
104	V1CH	0.02	-0.06	0.8480
105	L4PL	0.01	-0.06	0.8480
106	L2AB	0.03	-0.06	0.8480
107	HDTG	0.02	0.02	0.9491
108	V1FC	0.03	0.00	1.0000
109	L5PN	0.02	-0.02	0.9491
110	V1PL	0.03	-0.02	0.9491
111	L5AB	0.02	-0.02	0.9491
112	L4FC	0.02	0.02	0.9491

Table S6 – Ranked importance of the cytokines. Loadings of OPLS-DA and Cliff's delta of healthy vs SARS-CoV-2 positive patients.

Rank	Cytokine	Loadings from OPLS-DA	Cliff's delta	P value
OPLS-DA				
1	IL1-RA	0.36	0.99	5.88E-06
2	IP-10 (CXCL10)	0.39	0.86	9.22E-05
3	SDF-1 alpha	0.13	0.77	0.00034
4	IL-8 (CXCL8)	0.25	0.75	0.00034
5	MIP-1 beta (CCL4)	0.39	0.73	0.00071
6	IL-7	0.10	0.66	0.00201
7	MCP-1 (CCL2)	0.36	0.62	0.00379
8	RANTES (CCL5)	0.27	0.55	0.00965
9	TNF alpha	0.08	0.53	0.00965
10	IL-17A (CTLA-8)	-0.09	0.49	0.01671
11	IL-18	0.29	0.49	0.01852
12	IL-6	0.21	0.43	0.01619
13	IL-10:IP-10 (CXCL10)	-0.01	0.42	0.02344
14	IL-10	0.07	0.39	0.03385
15	IL-1 alpha	0.14	0.34	0.06845
16	IL-22	0.13	0.32	0.08640
17	IFN gamma	0.18	0.30	0.12205
18	Eotaxin (CCL11)	0.18	0.26	0.18337
19	IL-10:IL-6	0.14	0.26	0.08781
20	MIP-1 alpha (CCL3)	0.01	0.24	0.21494

Figure S1 (A) The principal component analysis (PCA) scores for healthy controls, SARS-CoV-2 positive and serology (+) samples from the CPMG spectra. The ellipse indicates Hotelling's T2 statistic ($\alpha=0.95$), which can be interpreted as a multivariate confidence interval. (B) Loadings of principal component 1. (C) Loadings of principal component 2.

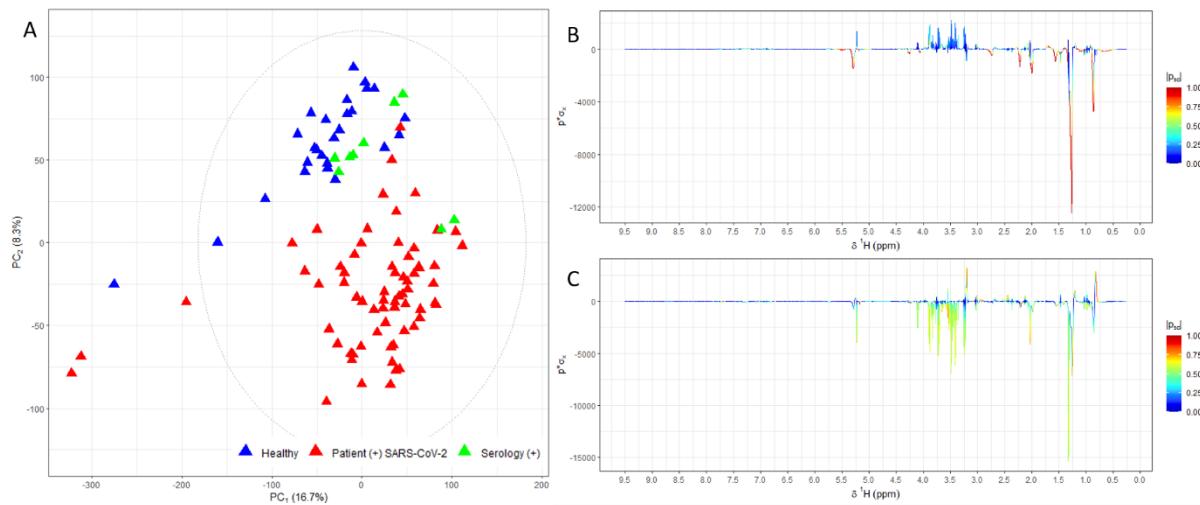


Figure S2 Glycoprotein A (GlycA) and glycoprotein (GlyB) NMR peak integrals for the healthy controls, SARS-CoV-2 positive patients and the SARS-CoV-2 negative patients.

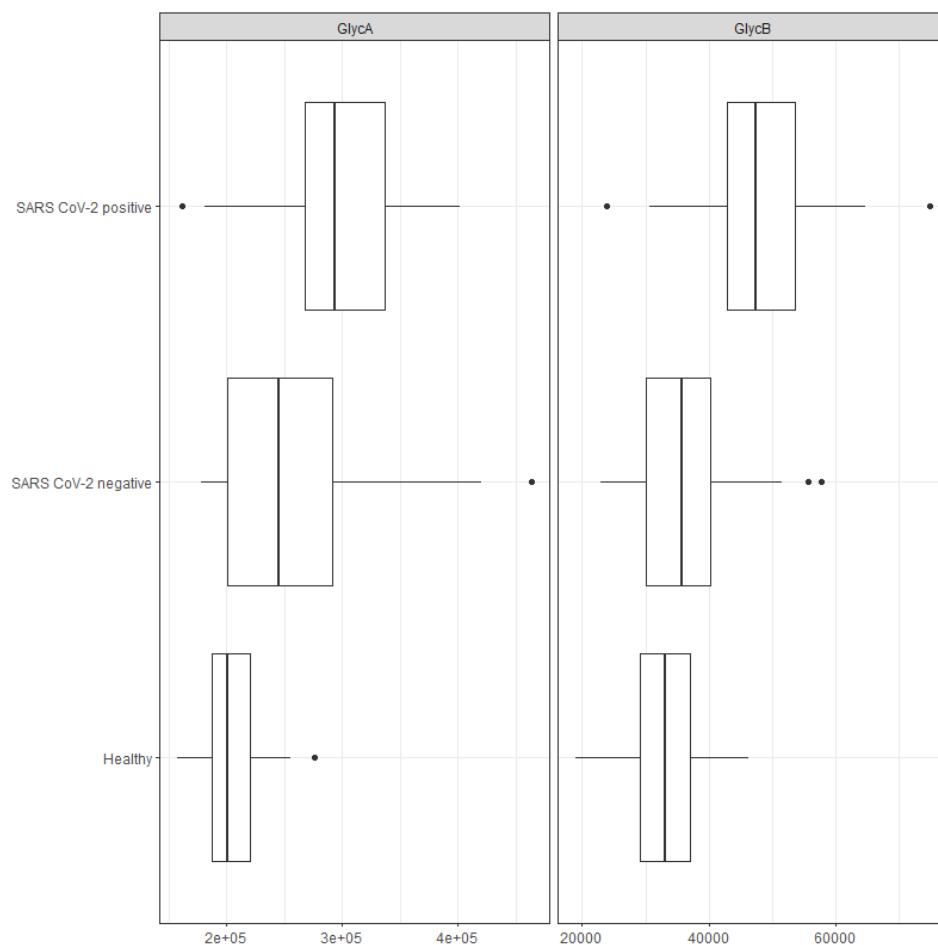


Figure S3 BMI regression against 1D spectrum showing high correlation with triglycerides and lactate.

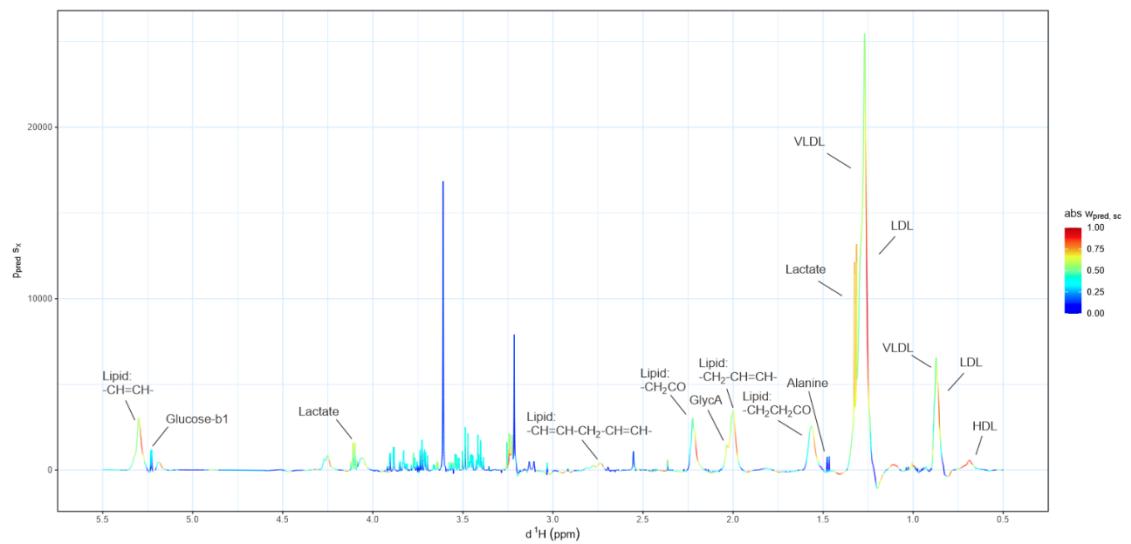


Figure S4 (A) OPLS-DA model plot showing the healthy controls and SARS-CoV-2 positive patients from the CPMG dataset. (B) The OPLS-DA loadings of the training set model. (C) All healthy samples projected into the model. (D) All SARS-CoV-2 positive samples projected into the model. (E) All SARS-CoV-2 negative samples projected into the model. (F) All serology (+) projected into the model.

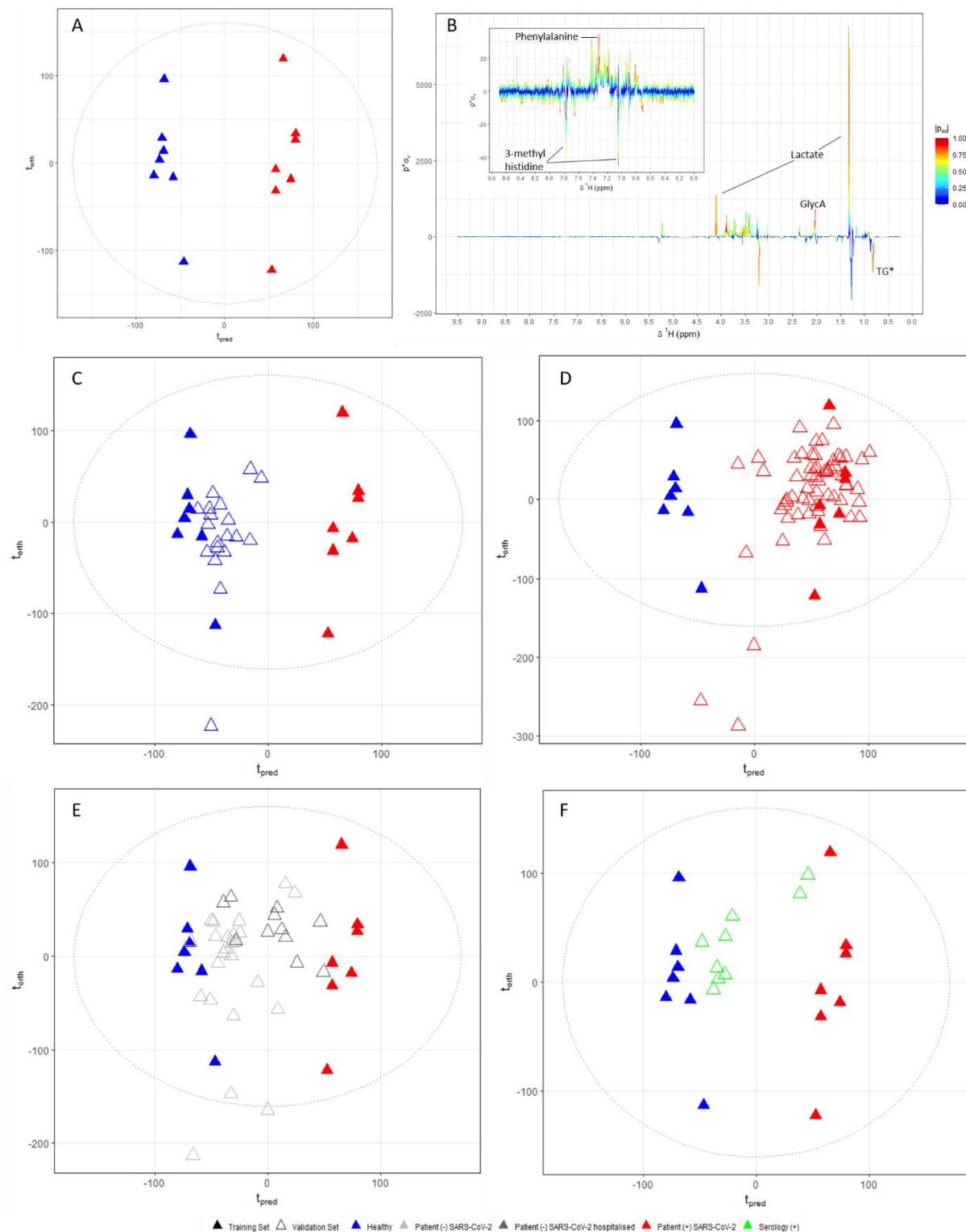


Figure S5 Overlaid zoomed in region (aromatic region) of the JRES spectra, healthy control in red and SARS-CoV-2 positive patient in blue.

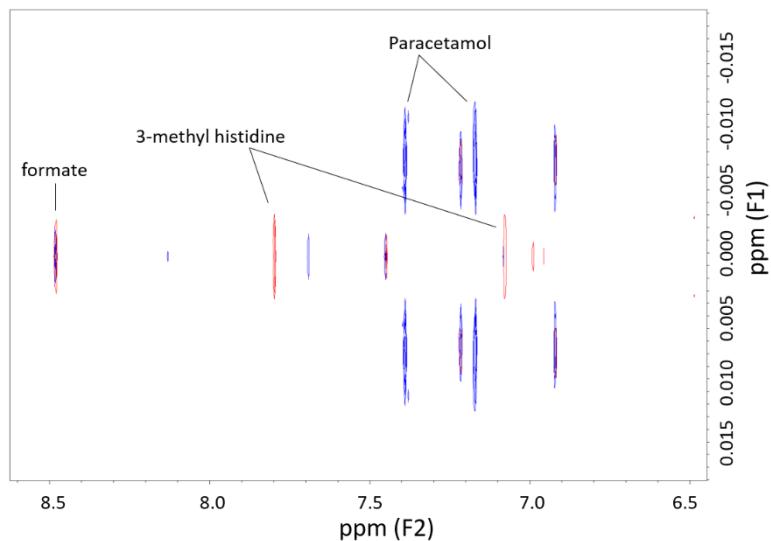


Figure S6 OPLS-DA analysis of lipoprotein and cytokine/chemokine data for the healthy and SARS-CoV-2 positive patients.

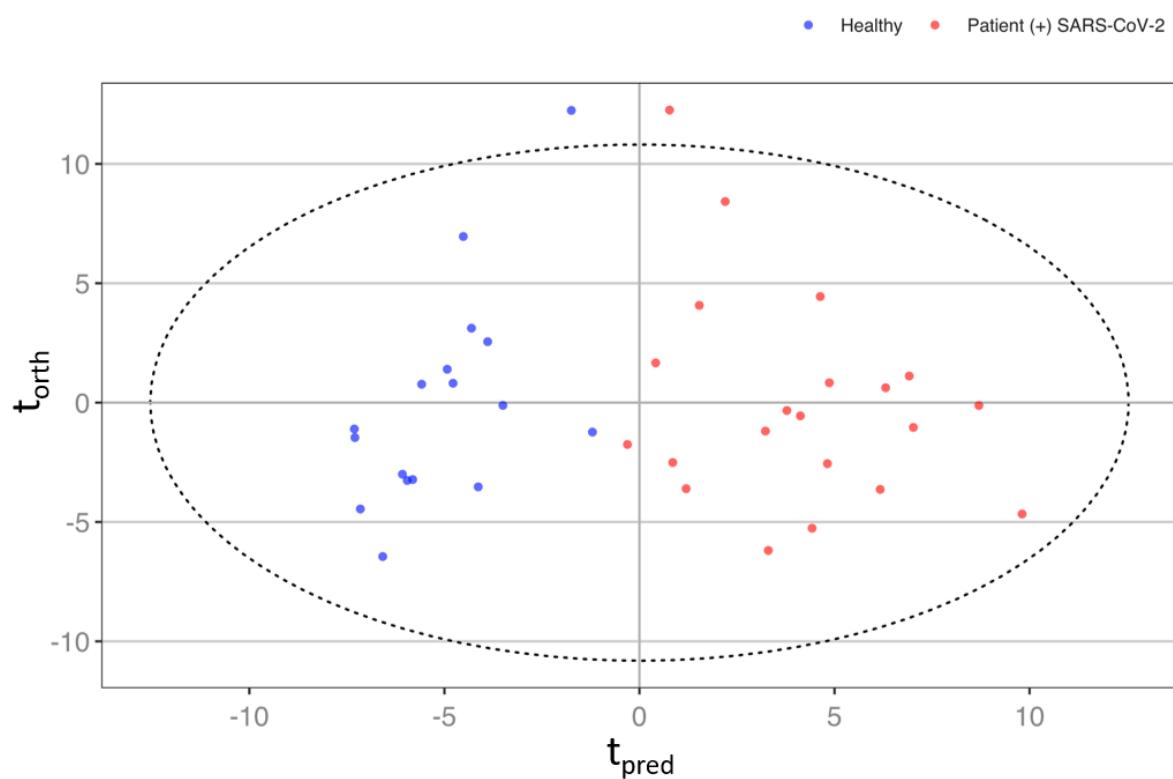


Figure S7 Box plots showing the cytokine and chemokine concentration of healthy (blue), SARS-CoV-2 negative (green) and SARS-CoV-2 positive (red) patients.

